Thyroid diseases

Thyroid hormone is important for metabolism in all body cells.

Physiology

- Thyroid produces → Mainly T_4 with ½ life of 7 days
  → T_3 with ½ life of 1 day
- T_4 is converted into T_3 in peripheral tissues [T_3 is the active form]
- Most of T_4 & T_3 are bound to plasma protein e.g. Thyroid-binding globulin TBG
- Pregnancy & OCP → ↑ in TBG → ↑ Total T_3 & T_4 but free T_3 & T_4 are normal.
- Nephrotic synd & Cirrhosis → ↓ TBG → ↓ Total T_3 & T_4 but free T_3 & T_4 are normal

Investigation of thyroid disease

- Pituitary thyroid-stimulating hormone [TSH] stimulates production of T_3 & T_4
- T_3 and T_4 inhibit the production of TSH
- Diseases of thyroid may be:
  1. Primary: thyroid disease → Hyperthyroidism → ↑ T_4 + ↓ TSH
     → Hypothyroidism → ↓ T_4 + ↑ TSH
  2. Secondary: Pit. disease → Hyperthyroidism → ↑ TSH + ↑T_4
     → Hypothyroidism → ↓ TSH + ↓T_4
- **TSH is most useful Ix of thyroid function** except when there is a Pit. disease

Goitre

- It is enlargement of thyroid.
- Pt may be → Hyperthyroid → Graves disease, Multinodular Goiter
  → Euthyroid → Simple diffuse goiter, Multinodular Goiter
  → Hypothyroid → Hashimoto thyroiditis
- Ultrasound is the most accurate method to assess thyroid size.
- WHO grading of goitre:

  Grade 0: No palpable or visible goitre.

  Grade 1: Palpable goitre (larger than terminal phalanges of thumbs).

  1 A Goitre detectable only on palpation.

  1 B Goitre palpable and visible with neck extended.

  Grade 2: Goitre visible with neck in normal position.

  Grade 3: Large goitre visible from a distance.

Clinical features		
	Hyperthyroidism	Hypothyroidism
General	**Hot intolerance** Gynecomastia Palmar erythema	**Cold intolerance** Effusions (pleural, pericardial, Ascites)
Gyne	**Amenorrhea** Infertility	**Menorrhagia** (rarely oligomenorrhea) Infertility
GIT	↑ **appetite** + Wt loss (rarely gain) **Diarrhea**	Weight gain **Constipation**
Muscle	Proximal myopathy Periodic paralysis (Asian pt)	Muscle cramps ↑Creatine kinase
CVS	Tachycardia **Atrial fibrillation** High-output cardiac failure Hypertension	Bradycardia **Ischemic heart disease** Hypercholesterolemia Hypertension
Neuro	Hyperreflexia Irritability Tremors Chorea	**Delayed relaxation** of Ankle reflexes Slow thinking & speech Cerebellar Ataxia Peripheral neuropathy
Eyes	**Lid retraction, lid lag**	**Periorbital edema**
Blood	Microcytic anaemia Leucopenia	Macrocytic or Normocytic anaemia If menorrhagia → Microcytic
Skin	**Sweating** Urticaria Hair loss Onycholysis [Plummer nails]	Yellow skin (due to caroteinaemia) Non-pitting LLE edema[myxedema] Hair loss including eyebrows Erythema ab igne
Lab	Hypercalcemia	Hyponatremia (due to ↑ ADH)
Other	Osteoporosis Glycosuria Lymphadenopathy ↑ Alkaline phosphatase	Deposition of mucopolysaccharides in: • Internal ear → Deafness • Vocal cords → Hoarseness • Wrist joint → Carpal tunnel synd

Hyperthyroidism

Etiology

1. **Graves disease** = diffuse toxic goiter [**most common cause**]
2. **Multinodular goiter**
3. **Toxic Hot nodule** [Plummer's disease]
4. Thyroiditis → Post-viral [de Quervain's]: Thyroid painful + ↑ ESR
   → Post-partum : self-limiting, no relation bw abnormal TFT & depression

Uncommon cause

1. Secondary: Excess production of TSH by pituitary tumor (very rare).
2. Thyrotoxicosis factiscia (exogenous intake of thyroxin) (Psychological problem)
3. Early Hashimoto thyroiditis
4. Ectopic thyroid tissue (strauma ovarii).
5. Drugs : Amiodarone.

Grave's disease ★ short case =-

Epidemiology: • ♀. 30-50 yrs
- Associated with HLA-B8, DR3
- Smoking ↑ the risk
- Association with other autoimmune diseases

Etiology: autoimmune disease with IgG Thyroid-stimulating immunoglobulin [TSI] binds to TSH receptors → diffuse goiter + ↑ thyroid hormone production

C/P: Features of hyperthyroidism + Features seen ONLY in Grave's but not in other causes of thyrotoxicosis:

- **Eye signs**: Exophthalmos, Ophthalmoplegia → diplopia. Optic nerve compression
  - The orbit contains excess glycosaminoglycans produced by fibroblast.
  - It affects 25-50% of pts. Pt may be eu-, hypo- or hyperthyroid
  - **Smoking & Radioiodine** Therapy → ↑ eye disease
  - Rx: Steroids, Radiotherapy, Surgery.
- **Pretibial myxedema** in ≤ 10% of pts, due to accumulation of mucopolysacchrides
- **Thyroid acropachy**: clubbing of finger
- Bruit over thyroid on auscultation is pathognomonic

Ix:

- TFT: ↑ T_4 & T_3 + ↓ TSH [Note: 5% of pts have Normal T_4 + ↑ T_3]
- Autoantibodies → **Anti-TSH receptor stimulating antibodies TSI** (95%)
  → Anti-thyroid peroxidase (microsomal) antibodies (50%)
- Diffusely ↑ **Radio-iodine uptake** Radioisotope scan.

Treatment

- β-blokers e.g. propranolol for symptomatic relief ↑HR - Diarrhea - sweating.
- **Antithyroid drugs: [Carbimazole, Methimazole, Propylthiouracil]**
  - They are given for 12-18 months.
  - When the drugs are stopped, relapse occurs in 50% of pt within 2 yrs and either surgery or radioiodine is used.
  - S/E of carbimazole: Skin rashes, Agranulocytosis (+Fever sore throat is 1st symptom) and pts must be warned to stop the drug and seek urgent medical advice.
- If medical treatment failed:
  - Subtotal thyroidectomy
  - Radioactive iodine ^{131}**I:** hypothyroidism rates 25% after 1 yr & 50% after 10 yrs

Note: after treatment of hyperthyroidism TSH may remain suppressed for Months

Multinodular goiter& Toxic adenoma

- Multinodular goiter is more in elderly & associated with arrhythmias & heart failure
- Remission is unlikely with anti-thyroidal drug, So Rx is β-blokers for symptoms and Radioactive iodine or surgery for thyroid disease

Thyrotoxicosis in pregnancy

- Thyrotoxicosis in pregnancy & breast feeding the drug of choice **Propylthiouracil**
- Subtotal thyroidectomy can be in the second trimester.
- Radioactive iodine is absolutely contraindicated in pregnancy & breast-feeding

Thyrotoxic crisis (Thyroid storm)

- Life threatening thyrotoxicosis with mortality rate of 10%.
- Precipitated by infection OR post-subtotal thyroidectomy OR ^{131}I therapy

C/P: **Fever, irritability,** confusion, tachycardia, AF ± heart failure. Vomiting & diarrhea

Rx: → Oxygen + IV fluid + Cooling hyperthermia > 39.5°C.

→ Antibiotics

→ β-blokers (Propranolol) for symptoms → ↓HR & AF

→ Propylthiouracil orally OR Carbimazole [carbimazole cab be given rectally] Propylthiouracil is better because is ↓ release & peripheral conversion of T_4 to T_3

→ Iodine : inhibit release and conversion of T_4 to T_3 [Sodium ipodate is an alternative and it restore serum T_3 levels to normal in 48-72 hours] temporary effect.

→ Dexamethasones: inhibit release and conversion of T_4 to T_3

Hypothyroidism

Etiology

1. Autoimmune disease
   - Hashimoto's thyroiditis: with Goiter
   - Atrophic hypothyroidism: no goiter
2. Post-thyroidectomy or ^{131}I Rx
3. Iodine deficiency → Radioactive Rx.
4. Drugs: Lithium
5. 2ndry to Hypopituitarism

Hashimoto thyroiditis

Epidemiology: 30-40 yrs ♀. The **most common cause for hypothyroidism.**

- Association with other autoimmune diseases e.g. Pernicious anemia, DM type 1, Addison, Vitilligo.

Etiology: autoimmune disease → chronic inflammatory process of the thyroid with lymphocytic infiltration of the gland. ↳ plasmacells.

Note: They have increased risk of thyroid lymphoma

C/P: Features of hypothyroidism ± Goiter which is painless.

Investigations

- TFT → ↓ T_4 & T_3 + ↑ TSH
- Autoantibodies → Anti-TSH receptor antibodies (20%)
  → Anti-thyroid peroxidase & Anti-thyroglobulin (90%)
  → ANA may be +ve
- Diffusely ↓ **Radio-iodine uptake**
- CBC: may be macrocytic, normocytic, or microcytic.
- ECG: bradycardia with low voltage complexes.

Note: Anti-thyroid peroxidase & Anti-thyroglobulin antibodies are present in 10-20% of normal population but in low titer.

Treatment

- T_4 [Thyroxin] supplement. Start at small dose then increase.
- Overtreatment is a risk factor for osteoporosis
- In pt with ischemic heart disease the lowest dose should be used initially, because exacerbation of ischemia → MI or sudden death are complications of thyroxine Rx
- In pregnancy → ↑ dose of Thyroxin

Myxedema coma

- Rare medical emergency with mortality rate of 50%
- *C/P*: decreased level of consciousness with:

  Hypothyroidism → T_3 IV + Precipitating factors: infection → antibiotic
  Hypothermia → gradual rewarming < 35°c
  Hypoglycemia → glucose IV
  Hypoventilation → O2 & ventilation + IV fluid for circulatory support
  Hydrocortisone → because it may 2ry & associated with ↓ cortisone

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L> to prevent addison crisis.

Asymptomatic abnormality in TFT

- **Subclinical Hypothyroidism**
  - ↑ TSH but T3, T4 normal
  - Pt have ↑ risk of AF & osteoporosis so they are treated [usually ^{131}I]
- **Subclinical Hyperthyroidism:** ↓ TSH but T3, T4 normal
- **Sick euthyroid syndrome:** during systemic illness TSH, T4 and T3 may be low. Changes are reversible upon recovery from the systemic illness.

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if high => pathological

Simple diffuse goiter

- It is enlargement of thyroid with no abnormality in TFT or antibodies → No Rx
- More common in ♀ bw 15 and 25 yrs & during pregnancy. Family history is +ve

Note: Presence of vocal cord paralysis, lymphadenopathy, and fixation to underlying or overlying tissues suggest malignancy and not simple goiter.

Riedel thyroiditis

- Rare fibrous induration of thyroid

Effect of iodine on thyroid status

- It may cause transient hypothyroidism (Wolff-Chaikoff effect)
- Hyperthyroidism (Jod-Basedow phenomenon).

Cushing syndrome

Definition: clinical state the occurs due to glucocorticoides

Etiology

- Iatrogenic (Cushinoid syndrome) **the most common cause.**
- Spontaneous
  1. ACTH-dependent
     - Pituitary adenoma (**Cushing disease**): 80% of spontaneous cases ♀>♂
     - Ectopic ACTH (bronchial CA) (small cell CA)
  2. ACTH-independent
     - Adrenal adenoma
     - Adrenal carcinoma
     - Adrenal hyperplasia
  3. ***Pseudocushing***: Alcohol, Depression, Obesity

* Chronic use of steroids.
1- RA
2- Asthma.

Clinical features

1. Disturbed metabolism of:
   - Fat → Moon-face: rounded face with bloated cheeks.
     → Central obesity with thin limbs
     → Buffalo-hump: ↑ fat in the interscapular region
   - Carbohydrate → Hyperglycemia, **DM** → Polydepsia & polyuria
   - Protein → Muscle: Proximal myopathy
     → Bone: Osteoporosis, Back pain
     → Skin: • Thin skin • Purple striae • Hirsutism • Acne • Bruises
2. Disturbed Electrolyte:
   - ↑ activation of aldesterone receptor → Hypernatremia → **Hypertension**
     → Hypokalemia & Metabolic alkalosis
3. Other:
   - Psychosis or depression
   - Polycythemia → plethora
   - Peptic ulcer
   - Infection
   - Impotence
   - Irregular menses

Note: ↑ ACTH may cause skin hyperpigmentation

Steroid Rx - no comedon.

Investigations

- CBC: ↑ Neutrophils & RBC, all other cells ↓ (Lymphopenia, Eosinopenia)
- Biochemistry: • Hyperglycemia • Hypernatremia • Hypokalemia • Metabolic alkalosis

➢ **Tests to confirm Cushing's syndrome** & exclude pseudo-Cushing's

1. Overnight-low dose dexamethasone suppression test (most sensitive)
   - If not Cushing → cortisol suppressed
   - If Cushing → cortisol is not suppressed
2. 24 hr urinary free cortisol

➢ **Test to Localize the site:**

1. ACTH level
   - If ↑ = ACTH dependent cause [Pit or Ectopic]
   - If ↓ = non-ACTH dependent [Adrenal adenoma or carcinoma]
2. High-dose dexamethasone suppression test:
   - if pituitary source then cortisol suppressed
   - if ectopic/adrenal then no change in cortisol
3. CRH stimulation
   - if pituitary source then cortisol rises
   - if ectopic/adrenal then no change in cortisol

Petrosal sinus sampling of ACTH may be needed to differentiate between pituitary and ectopic ACTH secretion

➢ ***Imaging:***

- MRI for pituitary
- Abd CT or MRI for Adrenla
- CXR or CT for Ectopic

Treatment

- Surgery is Rx of choice → Trans-sphenoidal resection for Pituitary tumor
  → bilateral Adrenalectomy for adrenal tumor

  If bilateral adrenalectomy is used in pts with Pituitary tumor it will to ↑↑↑ ACTH leading to skin hyperpigmentation and called Nelson's syndrome.
- Medical: Corticosteroid synthesis inhibitor: Metyrapone

Primary Hyperaldosteronism [Conn's syndrome]

Etiology:

1. Adrenal adenoma [most common cause]
2. Adrenal hyperplasia

Clinical features & Investigations

- ↑ activation of aldesterone receptor → Hypernatremia → **Hypertension**
  → Hypokalemia → Weakness
  → Metabolic alkalosis
- High serum aldesterone & **Low serum renin**
- Abd CT or MRI

Treatment

- Adrenal adenoma → Surgery
- Adrenal hyperplasia → Spironolactone → cause gynaecomastia.
  so change & give amiloride → no ~ & no hyperkalemia.

Note: In secondary hyperaldosteronism there is high renin → high aldesterone
① for eg- HF, cirrhosis, renal artery stenosis
↳ renal perfusion
② Diuretic Rx.

Adrenal insufficiency

Definition: Abnormal decrease in cortisol and/or aldosterone.

Etiology

➢ Primary Adrenal failure [**Addison's disease**]

1. **Autoimmune** adrenalitis is the **most common cause of Addison's disease.** More in ♀ and associated with other autoimmune disease e.g. Vitiligo in 20% of pts.
2. Infection: **TB** (Calcification on X-ray) _ HIV _ Fungal
3. Bilateral Adrenalectomy
4. Metastasis from lung or Breast CA
5. **Waterhouse-Friedrichsen synd:** adrenal hemorrhage in meningococcal sepsis

➢ Secondary Adrenal failure [due to low ACTH]

1. **Iatrogenic is the most common cause of adrenal insufficiency** [withdrawal of ch. glucocorticoid Rx → ACTH deficiency]
2. Pituitary disease

Clinical features

- ↓ aldesterone → Hyponatremia → **Hypotension** ↑H^+ => metabolic acidosis
- ↓ glocucorticoid → Hypoglycemia → **Weakness**
- ↓ androgen → loss of axillary hair in female
- **Abdominal pain,** ↓ Appetite & Weight loss.
- In Primary adrenal failure → ↑ ACTH → **Hyperpigmentation** of → Skin, Palmar creases, Buccal mucosa, Scars

[ACTH look like MSH melanocyte-stimulating hormone and stimulate malnocytes]

NOTE: Glucocorticoids depends on ACTH from pituitary. But Aldesterone depends on Renin-Angiotensin system [Not ACTH] So Aldesterone is affected only in primary failure

2ry => no hyperpigmentation & normal BP.

Investigations

- **Short synacthen test:** synthetic ACTH is given Once to stimulate cortisol. It is the Ix of choice. Cortisol levels will not ↑ in primary or secondary adrenal disease.
- Primary & Secondary can be differentiated by:
  - ACTH level: ↑ in primary & ↓ in secondary
  - **Long synacthen test:** ACTH for 3 days will stimulate cortisol if secondary
- Other tests:
  - **CBC**: neutropenia, lymphocytosis, and eosinophilia.
  - ↓ Aldesterone → Hyperkalemia, → Hyponatremia, → Metabolic acidosis
  - Hypercalcemia
  - Hypoglycemia
  - Urea is ↑ in primary disease but ↓ or Normal in secondary disease

Treatment

- Glucocorticoid replacement → Cortisol (hydrocortisone) is the drug of choice.
- Mineralocorticoid replacement in primary disease → fludrocortisones
- Pt should carry **Steroid card** at all times.
- Dose should be increased in case of stress [Surgery, Infections]

Acute adrenal crisis: Severe hypotension with hyponatremia ± hyperkalemia & hypoglycemia, Abdominal pain, **Vomiting**, Diarrhea. It is precipitated by surgery or infection. Rx: **IV** hydrocortisone, IV 0.9 Saline and 10% dextrose

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Pheochromocytoma

→ adrenaline.
→ nor "
→ dopamine.

Definition: A rare tumor of chromaffin tissue that secretes catecholamines. Mainly occurring in Adrenal medulla.

Rule of tens: • 10% malignant • 10% extra-adrenal • 10% familial • 10% bilateral

↳ sympathetic chain.

It is associated with MEN 2, Neurofibromatosis, von Hippel-Lindau syndrome

Clinical Picture

- **Triad** of Headache + Palpitation + Sweating
- **Hypertension** usually episodic [Attacks of postural hypotension are common]
- Pallor OR Flushing — Due dopamine release.
- Tremors
- Glucose intolerance → abdominal pain + vomiting + constipation + wt loss.

Investigation

1. Increased 24 hours Urinary Vanillyl-mandelic acid (VMA) OR metanephrine
2. Increased catecholamines (adrenaline and noradrenaline) OR metanephrine in plasma or urine.
3. Localization
   - CT or MRI abdomen
   - **MIBG** Meta-Iodo-Benzyl Guanidine scan: can detect chromaffin tissue tissues with overactivity

Treatment

1. Surgical removal of tumor is the Rx of choice
2. Medical Rx: Combined α-blocker [phenoxybenzamine] & β-blocker [Labetalol]
   - **α-blocker should be given first** [because if β-blocker is given first then all catecholamines will work on α-receptors → sever hypertension]
   - Used for pre- & post-operative period OR if surgery is not possible

Multiple-Endocrine-Neoplasia [MEN]

Endocrinal disorders characterized by ***tumors*** affecting many endocrinal glands with **Autosomal dominant**

MEN 1[Werner's syndrome]

- Primary hyperparathyroidism [Parathyroid hyperplasia]
- Pituitary tumors [Prolactinoma most common]
- Pancreatic neuro-endocrine tumours (e.g. insulinoma, gastrinoma)

MEN 2 [Sipple's syndrome]

- Primary hyperparathyroidism
- Medullary carcinoma of thyroid
- Pheochromocytoma

Autoimmune Polyendocrine Syndromes

Autoimmune disease affecting many glands and organs. They are 2 types:

1. Polyglandular syndrome type 1: (autosomal recessive) Characterized by:
    1. Mucocutaneous candidiasis
    2. Hypoparathyroidism
    3. Addison's disease
2. Polyglandular syndrome type 2= **Schmidt's syndrome:** (autosomal dominant) More in adult ♀, strongly associated with HLA-DR3.
    1. Addison's disease in all patients
    2. Autoimmune hypothyroidism
    3. Graves' disease
    4. Autoimmune Hypophysitis
    5. Type-1 diabetes,
    6. Primary hypogonadism
    7. Pernicious anaemia
    8. Vitiligo
    9. Celiac disease
    10. Myasthenia gravis

Disorders of Anterior Pituitary

According to size pituitary tumors are divided into:

- Microadenoma: < 1 cm
- Macroadenoma: > 1cm, may compress optic chiasm → Bitemporal hemianopia

Pituitary tumors
• Non-secreting tumor (usually macroadenoma) • Prolactinoma (commonest secreting pit. tumor) Micro in♀ Macro in♂ • GH secreting: Acromegaly (usually macroadenoma) • ACTH secreting: Cushing disease (microadenomas) • TSH secreting: 2ndy hyperthyroidism. Rare (microadenoma)

Hyperprolactinoma

Definition: Excess prolactin secretion from ant. Pit.

Etiolgoy

1. Pit. tumor
2. Physiological: Pregnancy, OCP, Lactation, Stress
3. Loss of inhibition by dopamine by drugs e.g. Antipsychotic, Antiemetics → metoclopramide (Plazil) + Peptic ulcer (cimetidine) (ask in history) TCAD
4. Increased stimulation by TRH (in hypothyroidism)
5. Polycystic ovary syndrome

Clinical features

- ♀: Galactorrhea is common, Oligo/amenorrhea, infertility
- ♂: Galactorrhea is rare, impotence, infertility ± features of macroadenoma

  Loss of hair ⇒ ↓ shaving.

Investigations

- ↑ Prolactin levels
- MRI brain

Treatment

- Medical: Dopamine agonist [**Bromocriptine, Cabergoline**] is **the first line of Rx**
- S/E: Nausea, Vomiting, Postural hypotension. → these may disappear within 1 or 2 yrs. Fibrosis in heart valve
- If medical ttt fails OR there is compressive symptoms (= macroadenoma) → trans-sphenoidal surgery
- Radiotherapy may be used to prevent regrowth after medical or surgical Rx

Done Echo every 6 month due to S/E of drug.

Acromegaly

Definition: clinical state due ↑ Growth hormone from pit. tumor (usually macroadenoma)

Clinical features :

- Skin
  - ↑ Sweating
  - Course
  - Oily skin
- Mouth
  - Separation of teeth
  - Large tongue
  - Prognathism
- Bones
  - Frontal bossing
  - Spade-like hands
  - ↑ shoe size
- Oraganomegaly
  - Goiter
  - hepatomegaly
  - Splenomegaly
- Macroadenoma
  - headaches
  - **Bitemporal hemianopia**
  - hypopituitarism
- Proximal myopathy
- ↑ prolactin in **1/3** of pt → galactorrhea

Complications

- Hypertension
- DM (10%)
- Cardiomyopathy
- Colorectal cancer
- Osteoarthritis
- Osteoporosis
- Carpal tunnel syndrome
- Obstructive sleep apnea

Investigations

- Growth hormone (GH) levels vary during the day and are therefore not diagnostic.
- Screening test → ↑ Serum **IGF-1** [Insulin-like growth factor]. It is produced by the liver under the stimulation of GH.
- Confirmatory test → **Oral glucose tolerance** (OGTT): Normal people will have GH suppression after intake of glucose but Acromegaly pt have **no suppression.**
- MRI brain.

Treatment

- **Trans-sphenoidal surgery is the treatment of choice**
- Medical Rx
  - Octreotide: somatostatin analogue (inhibits GH secretion)
  - Bromocriptine: dopamine agonist, (less effective than octreotide)
  - Pegvisomant: Growth hormone receptor antagonist

Hypopituitarism

Definition: combined deficiency of any of the anterior pituitary hormones.

Etiology

1. **Pituitary tumors** → Pituitary macroadenomas
   → **Craniopharyngiomas**: benign, from remnant of Rathke's Pouch. Rx is Surgical
2. **Sheehan's syndrome**: is hypopituitarism caused by infarction of the enlarged anterior pituitary during childbirth due to hypotension associated with bleeding.
3. **Pituitary apoplexy:** a sudden hemorrhage into a pituitary tumor. C/P: headache, neck stiffness, sudden blindness & hypotension. Rx: Steroid + Urgent surgery
4. Lymphocytic hypophysitis
5. Post-surgical
6. Uncommon causes: Infiltration [Sarcoidosis, hemochromatosis] TB

Clinical features & Investigations

Earliest lost → **Last lost**

	GH	FSH/LH	ACTH	TSH
C/P	Weakness ↑ body fat	↓ sexual hair Infertility Oligo/amenorrhea	Adrenal insufficiency	Hypothyroid
Ix	• **GH after stimulation** [**Insulin**, OR Arginine, Glucagon]	♂ Testosterone ♀ LH FSH	• **Short synacthen test** • **Insulin tolerance test**	• TSH ↓ • T4 ↓ T3 ↓
Rx	GH	♂ Testosterone ♀ Estrogen	Cortisol	Thyroxine

- Imaging: Brain MRI should be done to look for tumor

Insulin tolerance test

- Used in Ix of hypopituitarism to detect Growth hormone & Cortisol deficiency
- IV insulin given, GH and cortisol levels measured
- With normal pituitary function GH and cortisol should rise

Contraindications

1. Epilepsy
2. Ischemic heart disease
3. Sever adrenal insufficiency

Disorders of Posterior pituitary

Diabetes insipidus

Definition: problem with decreased function of anti-diuretic hormone ADH = Arginine Vasopressing AVP & it may be:

- Central diabetes insipidus: ↓ production of ADH
  - Etiology → Idiopathic
    → Tumor
    → Trauma [Usually transient]
- Nephrogenic diabetes insipidus: ↓ renal sensitivity to ADH.
  - Etiology → Lithium
    → Hypokalemia
    → Polycystic kidney disease

Clinical features

- Polyuria & Polydepsia [Up to 20 L of urine/day]

Investigations

- Urine has low specific gravity and osmolality.
- **Water-deprivation test**: To differentiate bw Cranial & Nephrogenic
  - 8 hours supervised with Hourly plasma osmolarity and urine osmolarity
  - Hourly wt [if > 3% of body weight loss stop the test]
  - Normal people will concentrate urine But pt with DI don't
  - If cause is cranial urine is concentrated after desmopressin

Response to Water Deprivation Test		
Initial Urine Osmolality < 300 mOsm/kg	After Dehydration Urine Osmolality > 600 mOsm/kg	After ↑ in Urine Osmolality > 600 mOsm/kg desmopressin
Normal	+	-
Cranial DI	No response	+
Nephrogenic DI	No response	No response

Treatment

- Cranial DI: Desmopressin (DDAVP): an ADH analog
- Nephrogenic DI: Thiazide OR Amiloride OR NSAIDs

Differential Dx of polyuria & Polydepsia

1. DM
2. DI
3. Hypercalcemia
4. Renal failure
5. Psychogenic polydepsia

Syndrome of inappropriate ADH [SIADH]

Definition: inappropriately ↑ production of ADH

Etiology

1. Lung diseases → Small cell carcinoma of the lung
   → Legionella Pneumonia (+hyponatremia)
2. CNS disease → Stroke
   → Trauma
3. Drugs: Carbamazepine, Chlorpropamide
4. Idiopathic

Clinical features: Symptoms of Hyponatremia: headache, confusion, seizure

Diagnosis.

1. Hyponatremia with Serum osmolality of less than 270 mOsmol/kg.
2. Inappropriately raised urine osmolality (> 150 mOsmol/l).
3. High urinary sodium of > 30 mmol/l
4. Exclusion of other causes

Treatment

- Fluid restriction to 500 to 1000 mL daily.
- If fluid restriction fails → Demeclocycline [It ↓ collecting duct responsivness to ADH]

Calcium disorders

- The three organs involved in calcium homeostasis are the bone (storage), kidney (excretion), and intestine (absorption).
- 3 hormones involved in calcium homeostasis:

1. **PTH** → ↑ Vit-D synth by the kidney; ↑ bone resorption; ↑ Renal Ca^{++} reabsorption; ↑ Renal phosphate excretion → ↑Ca^{++} + ↓ phosphate
2. **Vit-D** ↑ GIT absorption of Calcium & Phosphate → ↑Ca^{++} + ↑ phosphate
3. Calcitonin decreases serum calcium levels be depositing Calcium in bone

Hypercalcemia

Definition: Calcium level > 10.5 mg/dl

Etiology

1. Hyperparathyroidism → Primary & Tertiary [NOT Secondary]
   - Primary ↑PTH: There is ↑ PTH → Hypercalcemia
   - Secondary: Hypocalcemia [CRF, Vit-D ↓] → ↑ PTH
   - Tertiary: Prolonged ↓ Ca^{++} [CRF] → Hyperplasia of Parathyroid → ↑↑↑PTH → ↑↑ Ca^{++}
2. Tumor → bone marrow invasion → Multiple myeloma, Metastasis
   → Synth. of Parathyroid-related peptide → Squamous cell carcinoma of lung
3. Vit-D excess:
   - ↑Intake
   - ↑ Formation as in granulomatous disease e.g. • **Sarcoidosis** • TB
4. Thiazide
5. Others: • Immobiliztion • Milk-Alkali syndrome • Glucocorticoid deficiency

Management of Hypercalcemia

1. Rehydrate patient with iv N saline (0.9%). 4-6 L
2. Diuretics: after patient is rehydrated, continue N saline infusion and add **Frusemide**
3. Bisphosphonates: inhibit osteoclast activity → ↓ plasma Ca^{2+}. [e.g. Pamidronate]
4. Steroids: Most effective in Vit-D excess [Sarcoidosis], and malignancies
   - Other drugs that may be used: Calcitonin. Mithramycin
   - If the pt has renal failure consider dialysis

Primary hyperparathyroidism

Epidemiology

- More in ♀ > 50 yrs
- It is Associated with multiple endocrine neoplasia: MEN I and II

Etiology

- Solitary adenoma (80%) commonest cause of hyperparathyroidism & hypercalcemia
- Multiple adenomas
- Hyperplasia (15%)
- Carcinoma

Clinical features – [Bones, Stones, abdominal groans and psychic moans]

- 50% of pts are asymptomatic
- Polydipsia, polyuria [Severe Dehydration may occur]
- Abdominal: • Pain • Peptic ulceration • Constipation • Pancreatitis
- Bones → Bone pain/fracture
  → Bone cysts: Osteitis fibrosa cystic [Brown tumors]
  → Resorption of phalanges
- Renal stones, Nephrocalcinosis
- Depression
- **Hypertension**
- Impaired glucose tolerance

Investigations

- PTH is raised → Raised calcium + Low phosphate + ↑ Alkaline phosphatase
- X-ray → Skull: pepper-pot appearance
  → Hands: Terminal resorption of phalanges
  → of Joints: Chondrocalcinosis
- Localization: Technetium-MIBI subtraction scan

Treatment

- Surgical: Total parathyroidectomy
- Surgery is indicated for Pts < 50 yrs with **symptoms** or complications e.g. PU. Renal stones. Osteopenia
- Hungry bone syndrome: hypocalcemia after removal of adenoma Rx: Calcium

Milk-Alkali syndrome: It is due to ingestion of large quantities of calcium and absorbable alkali. Leading to Hypercalcemia, Systemic alkalosis, and Nephrocalcinosis.

- milk + antiacid (alkali)

Hypocalcemia

Definition: Calcium level < 8 mg/dl

Notes:

- 50% of Ca^{2+} ionized [active form] & 50% is non-ionized or protein-bound [not active].
- Total Ca^{2+} level should be corrected the level of albumin by adding 0.8 mg/dl of Ca^{2+} for each 1 mg/dl of albumin reduction below 4 mg/dl.
- In presence of Alkalosis Ca^{2+} will from ionized to non-ionized → Symp of hypocalcemia

Etiology = DDx of Tetany

1. Hypoparathyroidism
2. Vit D deficiency → In children → Rickets'
   → In adults → Osteomalacia
3. **Renal failure** (most common cause for hypocalcemia)
4. **Alkalosis**: e.g. Resp. alkalosis due to hyperventilation asthma, or PE.
5. Hypomagnisemia
6. Acute pancreatitis

Clinical features

- **Perioral** and peripheral numbness
- Tetany is defined as increased excitability of peripheral nerves.
- **Tetany**
  - → Manifest → Carpal-pedal spasm: Flexion of MCP with Extension of IP
    → Laryngospasm → Stridor
  - → Latent → **Chvostek's sign**: tapping facial N → twitching of facial ms.
    Trousseau's sign: Inflation of a sphygmomanometer > systolic BP for 3 minutes → Carpal spasm.
- **Seizures**
- Prolonged QT interval → Arrhythmias
- Prolonged may → Cataract
- Hypertension may occur

Treatment

- If the cause is alkalosis → Rebreathing expired air in a paper bag or closed mask.
- 10 ml of 10% Calcium gluconate very slowly IV over 10 minutes

Hypoparathyroidism

Etiology

- Post-thyroidectomy [commonest cause of hypoparathyroidism]
- Autoimmune hypoparathyroidism
- Congenitally absent [DiGorge syndrome]

Clinical feature: As above

Investigations

- X-ray of skull: Calcification of the Basal ganglia
- PTH is reduced → Low calcium + Raised phosphate

Treatment

- Oral calcium + Vit-D analogues e.g. 1,25-dihydroxycholecalciferol (calcitriol).

Pseudohypoparathyroidism

Definition: a hereditary disease which is characterized by:

1. Resistance of kidney & bones to the action of PTH → ↓ Calcium & ↑ Phosphate
2. Skeletal abnormalities (**Albright's hereditary osteodystrophy**): Short stature, with shortening of the 4th metacarpal & metatarsal bones.

Skeletal abnormalities may occur without PTH resistance = Pseudopseudohypoparathyroidism

Ix: PTH is elevated (or normal) with Low calcium + Raised phosphate.

Rx: As hypoparathyroidism

Osteomalacia

Definition: clinical picture caused by Vit-D deficiency in Adults

C/P:

- Bone Pain and tenderness.
- Proximal myopathy mainly affecting the legs.

Ix:

- Low Vit-D → Low Calcium + Low Phosphate + ↑ Alkaline phosphatase
- X-ray: **Looser's zones** = Pseudofractures

Rx: Vit-D supplement

Diabetes Melitus

It's metabolic syndrome characterized by inability of the body to decrease the level of glucose in the blood

Function of insuline

- anabolic hormone
- ↓ ketogenisis
- ↑
- ± lipogenisis ↑
- ↑ glycogenisis
- ↓ lipolysis

Diabetes mellitus

Definition: It is a clinical syndrome characterised by chronic hyperglycemia at levels sufficient to cause microvascular complications & the hyperglycemia may be due to absolute or relative deficiency of insulin.

Epidemiology

- Most common cause of blindness in age group 20-65 years
- Most common cause for lower limb amputation.
- Most common cause for CRF

	Type 1 IDDM	**Type 2** NIDDM
Epidemiology	10% of cases Age < 40 ♂ > ♀ More in Caucasians	85 % of cases Age usually ≥ 20 [Except MODY] ♂ = ♀ More in Asian, Black
Genetics	Both parents affected 30% risk Identical twins: 50% concordance HLA DR3/4, DQ8 Association	Both parents affected: ~~90%-100%~~ risk 60% Identical twins: up to 90% concordance No HLA association
Etiology	Autoimmune damage of pancreatic β-cell	Insulin resistance of unknown origin not all autoimmune
Antibodies	90% of pt have anti-islet cell antibodies	No Associated antibodies Amyloid deposition in islets of pancreatic cells
Metabolism	**Ketosis prone**; Absolute insulin deficiency	**Ketosis-resistant**; insulin levels may be high, normal, or low
Clinical features	Normal or low body weight	Usually obese Acanthosis nigricans often asymptomatic
Treatment	Insulin associated with other autoimmune diseases	Weight loss ± Oral agents OR Insulin

use arabic number

5%

2y DM

Risk factors for DM type 2:

- Acanthosis nigricans • Gestational DM • Polycystic ovary synd.
- Diagnostic Features of Metabolic Syndrome X (≥ 3 the following) MCQ
  1. Abdominal obesity (waist circumference: men > 102 cm, women > 88 cm)
  2. Hypertriglyceridemia (≥ 150 mg/dL) - hyperviscosemia
  3. Low HDL cholesterol (men < 40 mg/dL, women < 50 mg/dL)
  4. Hypertension (≥ 130/85 mmHg) - raised fibrinogen
  5. Fasting hyperglycemia (≥ 110 mg/dL) - hyperinsulinemia

Clinical features

- Asymptomatic "accidental diagnosis"
- Signs & complication of DM
  - blurring of vision
  - Neuropathy
  - Ischemic vascular changes
  - Recurrent infection

❖ 5% of DM are due to secondary causes:

1. Endocrinal diseases [Anti-insulin hormones]
   a. Glucagonoma – polydipsia – polyuria – Glucagon
   b. Cushing's syndrome – Cortisol
   c. Acromegaly – Growth hormone
   d. Pheochromocytoma – Catecholamines
   e. Thyrotoxicosis – Thyroxine
2. Pancreatic damage: DM occurs when > 80% of pancreas is damaged
   a. Ch. pancreatitis
   b. Hemochromatosis
3. Gestational diabetes (50% diabetic in 10 years)
4. Drugs: • Thiazides • Cortisol

– Dysacchariamia tonyca
– Freidrik ataxia

Clinical features

- **Polydepsia & Polyuria** + **Nocturia** [due to osmotic diuresis]
- **Weight loss** despite **Polyphagia** [Mainly in DM Type 1]
- Weakness
- **Infections** of the skin, vulva, and urinary tract.
- Blurring of vision: due to changes in optic lens shape due to hyperglycemia.

➢ Symptoms of Ketosis: [Occur mainly in type 1 DM, & very rarely in type 2DM]

- Abdominal pain & vomiting
- Kussmaul breathing
- Acetone smell

[↓ insuline ⟹ enters K⁺ & glucose to the body.
↑ insuline ⟹ glucose enter to the cells.] ← anti insuline hormon secreted if to the cells glucose not entered to cells. ↑ present.

(cortisol). (GH). (catecholamine)

↓

go to liver (carbohydrate – fat – ↓ glycogenolysis –

Protein ↓ gluconeogenesis.

(glucose + keton body

The main differance bw DM1 & DM2 ⟹

* Small amount of insulin inhibit lipolysis.

Ketone body not formed.

- Blood Tests

  Fasting > 126

  Random ≥ 200

- Urine test

  ~~glucose~~ - glycosuria

  - ketonuria

- Lipid profile

- 24 hour urine collection to check for microalbumin urin (normally less than 30)

- Funduscopy to check the retina

- Blood pressure

- BMI

- Haemoglobin A1c

Diagnosis of DM

Values are based on venous plasma.

- **With symptoms** [Polydepsia, Polyuria]: **Fasting glucose >7.0 mmol/l** OR **Random glucose >11.1 mmol/l** OR a glucose of >11.1 mmol/l 2 hours after 75 g GTT
  [GTT to be performed when fasting glucose is > 6 mmol/l and, if diabetes is suspected, when random blood glucose is <11.1 mmol/l]
- **Without symptoms:** Either Fasting glucose >7 mmol/l OR random glucose >11.1 mmol/l, present on two occasions.
  - 7 mmol/l = 126 mg/dL
  - 11 mmol/l = 200 mg/dl

Diagnosis of Impaired glucose tolerance (Prediabetes)

- **Impaired glucose tolerance:** 2-hour GTT glucose > 7.8 mmol/l but < 11.1 mmol/l
  > 140 mg/dL but < 200 mg/dL

- **Impaired fasting glucose:** Fasting glucose > 6.1 mmol/l but ≤7.0 mmol/l
  >110 mg/dL but ≤126 mg/dL

Impaired glucose tolerance ≠ Hyperglycemia. Pt with Impaired glucose tolerance don't have ↑ risk of microvascular disease, but it ↑ the risk of macrovascular complications.

20% of pt with IGT will progress to type 2 DM within 5 years

Hemoglobin A_{1c} (glycosylated hemoglobin)

- HbA_{1c} measures the average serum glucose concentrations over the prior 2-3 months.
- It is NOT used for Diagnosis only for follow up
- Ideal goal for HbA_{1c} is < 7%
- ↑ HbA_{1c} is associated with ↑ microvascular complication [not macrovascular]

every increase in HbA1c by 1% it equals 2 mmol/l

So if patient has HbA1c 13% it means that the patient had blood glucose level 13 mmol/l = 352 mg/dl

Treatment of DM type 1

- All pts require insulin replacement + Life-style changes as type 2
- Oral hypoglycemia are not used.

Treatment of DM type 2

1. **Life-style** [aim for ideal body weight as Obesity increases insulin resistance]
   - ➢ **Dietary advice** → ↓ refined carbohydrate and ↑ complex carbohydrate intake.
     - → Reduce saturated fat.
     - → Avoid excessive alcohol.
   - ➢ **Exercise**
2. **Oral hypoglycemic agents**

Drug	Mode of Action	Side-effects	Contraindications
Sulphonylureas: ★ • Gliclazide • Glibenclamide • Tolbutamide	• ↑ insulin release [block K^+ channel in β-cell of pancreas causing its depolarization]	• Weight gain • Hypoglycemia	
Biguanides: ★ • Metformin	• ↓ hepatic gluconeogenesis • ↓ insulin resistance	• GIT upset • **Lactic acidosis**	• **Renal failure** • Heart failure
Thiazolidinediones: • Rosiglitazone • Pioglitazone	• ↓ insulin resistance by activating (PPAR-γ) Peroxisome proliferator-activated receptor	• Hypoglycemia • Hepatotoxicity • Fluid retention	• Heart failure
Meglitinides: • Repaglinide • Nateglinide	• ↑ insulin release	• Hepatotoxic • Hypoglycemia	
α-Glucosidase inhibitors: acarbose	• ↓ carbohydrate digestion	• Bloating • diarrhea	

- Metformin is the drug of first choice in overweight patients
- Sulphonylureas are considered for patients who are not overweight, or in whom metformin is contra-indicated or not tolerated.

How to give insulin?

- subcutaneous injection
- ant. abdominal wall, thigh, deltoid, buttock area
- change the site of inj injection

Regimes of treatment

- Twice daily 2:1 = 2 intermediate : 1 short "mixed"
- 3 dose soluble insulin be 30 min before each meal + an intermediate acting insulin at bedtime

✱Hypoglycemia

When blood sugar ↓ less than 50 mg/dl

- neuroglycopenic symptoms "confused, headache, fatigue, disoriented"
- stimulation to catecholamines "sweating, palpitation, nausea, shivering"

treat the patient with sweet "monosaccharide" dramatical recovery

Causes of hypoglycemia

- not eating
- mal absorption
- over dose
- insulinoma
- poor regime
- Lipohypertrophy
- hepatic or renal problems
- hypoadrenalism, hypopituitarism

3. **Insulin:** 30% of type 2 DM will require insulin people with type 2 diabetes.
Regimes for giving insulin:
- Twice daily regime of Mix of Short-acting & Intermediate-acting insulin (NPH).
- Multiple injection regimens: Basal Glargine which cover 24 hrs with short-acting insulin being taken before each meal

Insulin	Onset	Peak	Duration
Rapid-acting • Lispro • Aspart	< ½ hr	1 hr	4 hr
Short-acting • Soluble (Regular)	1 hr	3 hr	8 hr
Intermediate-acting: • Isophane (NPH) • Lente	2hr to 3hr	8 hr	16 hr
Long-acting: • Ultralente • Glargine	6 hr 1hr	16 hr **No Peak**	24 hr 24 hrs

Side-effects of insulin
1. Hypoglycemia
2. Weight gain
3. Peripheral edema (insulin → salt and water retention)
4. Lipodystrophy at injection sites & lipohypertrophy
- rely allergy

Special situations

- ***Honeymoon period:*** a **temporary** phase in the first 1-2 yrs after the onset of DM type 1. There is temporary improvement in β-cell function → hypoglycemic attack → reduction in the dose of exogenous insulin.
- **Somogyi effect: Insulin-induced hypoglycemia** (↑ insulin dose - at night) → release of counterregulatory hormones such as epinephrine and glucagon → **Rebound Morning Hyperglycemia.** Pt usually have nightmares. Rx: ↓ the dose of evening NPH. in the morning.
- ***Dawn phenomenon:*** **Morning hyperglycemia** due to early morning circadian release of cortisol, growth hormone, & catecholamines. Rx: ↑ the dose evening NPH.

Recommended goals for glycemic control in patients with DM
- Hemoglobin A_{1c} < 7%
- Preprandial glucose 90-130 mg/dL
- Postprandial glucose < 180 mg/dL

Complications of DM

- ***Microvascular***
  1. Retinopathy (90%)
  2. Neuropathy (70%-90%)
  3. Nephropathy (30%-40%) usually within 20 yrs of onset of disease.

- Microvascular complications take minimum of 5 years to develop, even with poor glycemic control.
- Tight glycemic control may decrease the risk of Microvascular complications by 50%

- ***Macrovascular***
  1. Ischemic heart disease (accounts for 70% of deaths in DM pts)
  2. Peripheral vascular disease
  3. CVA, hypertension

- Macrovascular complication which is responsible for most of the increased mortality in DM. It is not closely related to the glycemic control → The Aim of management is to reduce other risk factors for IHD:
  1. BP control. The goal is < 130/80 mmHg. First-line drug is ACE inhibitors.
  2. Smoking cessation.
  3. Lipid Rx: Test annually. Goals: LDL < 100 mg/dL, triglycerides < 50 mg/dL, and HDL > 40 mg/dL.
  4. Consider aspirin therapy for primary or secondary prevention.
  5. Consider screening for coronary artery disease.

Screening

- Screening is annual & Started after 5 yrs of Dx for DM type 1 & at time of Dx for DM type 2.
- **Diabetic nephropathy:** Screen for Microalbuminuria [30-299 µg albumin/mg creatinine]
- **Diabetic retinopathy:** by ophtahlmologiest

Vaccination

- Annual influenza vaccine should be given to all pts with DM.
- Pneumococcal vaccine is recommended for all diabetic adults at least once.

Diabetic Retinopathy → treatable.

- Background or non-proliferative retinopathy → follow up
- Proliferative retinopathy → laser photocoagulation
- 50% of visual loss in type 2 DM is due to causes other than diabetic retinopathy. e.g. cataract,

Diabetic Nephropathy → treatable

- ***Stages:*** ↑GFR → Microalbuminuria → albuminuria → Nephrotic syndrome → ESRD
  (asymptomatic stage. (30-300mg) to 3gm.)
- Control of blood pressure & ACE inhibitor reduced the progression renal disease.

→ End stage Renal disease.

Diabetic Neuropathy not treatable.

- Polyneuropathy
  - Symmetrical sensory with stocks distribution ± gloves ± Charcot's joints
  - Asymmetrical, mainly motor
- Mononeuritis multiplex: commonly CN III [pupil is spared] oculomotor nerve.
- Diabetic amyotrophy: Quadriceps wasting + painful skin.
- Autonomic neuropathy ↓ sympathetic activity.
  - Postural hypotension
  - Gastroparesis food lasting in stomach > 5hrs.
  - Diarrhea or Constipation
  - Impotence 50% in 5yr of the disease.

Examination of DM pt:

- Look for Postural hypotension
- Examine Eyes by ophthalmoscope
- Look for Site of injection
- Lower limbs for • Infection • Peripheral pulses • Sensory changes

Acute complications of DM

Diabetic Ketoacidosis & Hyperosmolar Hyperglycemic state

- DKA is seen mainly type 1 DM and HHS mainly in type 2 DM. But DKA may occur in severe cases of type 2.
- DKA is associated with absolute Insulin deficiency [type 1DM] & HHS is associated relative Insulin deficiency [type 2 DM]
- Ketosis does not develop in HHS because these pts have enough insulin to suppress lipolysis & ketogenesis, but not enough to prevent the liver from producing glucose.
- In both hyperglycemia → Volume depletion

Laboratory Changes in DKA and HHS		
Investigations	DKA	HHS
Glucose	250-600	600-1200
Sodium	125-135	135-145
Potassium	Normal or ↑	Normal
Osmolality (mOsm/ml)	300-320	330-380
Plasma ketones	++++	Normal or Slightly +
Arterial pH	6.8-7.3	> 7.3
Arterial Pco_2	20-30	Normal
Anion gap	↑	Normal to slightly ↑

Precipitating factors for DKA and HHS

1. Inadequate insulin administration
2. Infection (pneumonia, UTI, gastroenteritis, sepsis)
3. Infarction (cerebral, coronary, mesenteric, peripheral)
4. Surgery
5. Drugs (cocaine)

DD of breath odor

- aceton → DKA
- almond like odor → cayanide toxicity
- urine heater → renal fever
- garlic → organophosphates

Diabetic ketoacidosis

Clinical feature

- Polyuria, Polydepsia, & weight loss. → ketonuria
- Anorexia, nausea, vomiting, and abdominal pain. blurred vision
- Kussmaul respirations and an acetone odor on the pt's breath.
- Vital signs: ↑ HR, ↓ BP, ↑ RR, ± Fever weak pulse, cold extremities
- Altered mental function, or even coma. - electrolyte disturbance

Investigations:

- RBS → Hyperglycemia [The degree of hyperglycemia does not correlate with the severity of the metabolic acidosis]
- Plasma & Urine ketone (β-hydroxybutyrate, & acetoacetate) +++
- ABG: Metabolic acidosis (arterial pH 6.8–7.3).
- WBC: Leukocytosis is common due to stress → ↑ cortisol → neutrophilia
- ALL pt have a total-body potassium deficit, but the serum potassium at presentation is usually high due to acidosis. or normal.
- The measured serum sodium is reduced as a due to hyperglycemia.

↑ α amylase doesn't mean problem with pancreas

Complications of DKA

1. Cerebral edema [it has high mortality, more in children, associated with rapid reduction of blood glucose and use of bicarbonate, and is Rx with mannitol]
2. Acute respiratory distress syndrome
3. Thromboembolism
4. Disseminated intravascular coagulation (rare) DIC
5. Acute circulatory failure

DKA Prognosis: Mortality about 10%.

Hyperglycemic Hyperosmolar State

Clinical features

- Typically an elderly pt with Polyuria, thirst, weight loss ± ↓ level of consciousness.
- Symptoms of Vomiting, Abdominal pain & Kussmaul respirations are ABSENT.

Investigation (see table above)

Treatment is the same as DKA except that they need **Less insulin**

- The pts have high risk of thrombosis → Prophylactic insulin **Heparin**

* (due to dehydration)

HHS Prognosis: Mortality rate about 40% due to the presence of other disease e.g. IHD

Management of DKA

- **Admit to hospital.**
- **Replacement** "Rehydration"
  1. **Fluids**:
     - 0.9% saline (NaCl) I.V
       - 1 liter over 30 minutes
       - 1 liter over 1 hr
       - 1 liter over 2 hrs
       - 1 liter over 4 hrs
       - 1 liter 8-hourly
     - When blood glucose 270 mg/dl
       - Switch to 5% dextrose, ∫to ↓ risk of brain edema]
     - Typical requirement is 6 liters in first 24 hrs.
  2. **Electrolyte (K):**
     - If pt plasma potassium is <3.5mmol/L or normal 3.5-5 mmol/L. Give K^+
     - If pt is hyperkalemia ≥5.0mmol/L. Don't give until it falls to normal range
     - Avoid K^+ infusion rate of > 20 mmol/hr
  3. **Sodium bicarbonate** (1.4%): may be given if arterial pH is 6.9 or less.
  4. **Administer regular insulin**:
     - 50 units soluble insulin in 50 ml 0.9% saline I.V. via infusion pump
       - 6 units/hr initially
       - 3 units/hr when blood glucose < 270 mg/dl
       - 2 units/hr if blood glucose declines < 10 mmol/l (180 mg/dl)
       - Administer intermediate or long-acting insulin as soon as patient is eating.
       - Allow for overlap in insulin infusion and subcutaneous insulin injection.
- **Monitoring:**
  - Blood glucose every 1–2 h.
  - Urea & electrolytes (mainly K^+) & ABG every 4 h for first 24 h.
  - BP, pulse, respirations, mental status, and fluid intake &output every 1–4 h.
- **Investigate for the cause:** ECG, CXR, CBC, CRP
- Antibiotics if infection is present.

note: * at 1st half hr of supplementation of S/C insuline injection let the insuline infusion pump B/C the ~ ~ ~ take ½ hr to be act.

Hypoglycemia

Definition: blood glucose levels < 50 mg/dl

All DM pt should be educated about the symptoms of hypoglycemia

Clinical features:

- ↑ sympathetic activity: • Sweating • Tremor • Tachycardia • Anxiety • Hunger
- Neuroglycopenic symptoms: • Dizziness • Headache • Confusion
  • Seizures • Focal neurological deficit • Coma

Rx:

- Conscious → Oral
- ↓ level of consciousness → 50 ml 50% dextrose IV
- If no vein can be canulated → Glucagon IM

	DKA	Hypoglycemia
History	Missed insulin	Missed meal
Onset	Slow	Rapid
Skin & Tongue	**Dry**	**Moist**
Pupils	Normal	**Dilated**
Respiration	**Kussmaul's**	Normal
Breath	**Acetone**	Normal
Pulse	Weak & Rapid	Good
BP	Low	High
Symptoms	Abdominal pain	no
Urine	Glucose & acetone	Normal
Blood glucose	High	Low
Response to glucose	No effect	Rapid improvement

DDx of Hypoglycemia unrelated to diabetes

1. Insulinoma
2. Factitious (insulin or sulphonylurea)
3. Adrenal insufficiency
4. Alcohol
5. Severe liver failure
6. Salicylate poisoning

Note: Endogenous insulin is secret with C-peptide But Exogenous insulin has no C-peptide

Gynecomastia DDx:

1. Puberty
2. Obesity
3. Idiopathic
4. ↑ Esterogen: Liver cirrhosis. Hyperthyroidism
5. Drugs: • Digoxin • Spironolactone • Cemitidine • Estrogen

Hirsutism DDx:

1. Idiopathic [most common cause]
2. Drugs: • Cyclosporin • Minoxidil • Androgen • Cortisol
3. Ovarian: • Polycystic ovary syndrome • Ovarian tumor
4. Adrenal: • Cushing disease • Congenital adrenal hyperplasia

Hypertriglyceridemia DDx:

1. Alcoholism
2. Obesity
3. Ch. Renal disease
4. Liver disease
5. DM
6. High-dose estrogen

Hypercholesterolemia DDx:

1. Hypothyroidism
2. Cigarette smoking
3. Nephrotic syndrome
4. Cholestatic liver disease [e.g. primary biliary cirrhosis]